

**REMARKS**

Applicants request reconsideration of the present application in view of the reasons that follow.

**I. Status of the Claims**

Claims 1-16, 18-20, 22-29, and 31 were cancelled previously. Claims 17, 21, and 30 are pending. No claims are presently cancelled or amended.

**II. Response to the Office Action**

Applicants gratefully acknowledge the PTO's withdrawal of the previous objections to the specification and claims and the section 112 and 101 rejections. At issue are two maintained grounds for rejection that Applicants address in the order presented. *See* Office Action at page 2.

**A. The Claims Are Not Anticipated by Wiley**

The PTO maintained its rejection of claims 17, 21, and 30 under 35 U.S.C. § 102(b) for alleged anticipation by U.S. Patent Application Publication No. 2002/0041876 to Wiley *et al.* ("Wiley"). *See* Office Action at page 3. The PTO rejected Applicants' previous arguments in asserting that Wiley teaches administering an antisense nucleic acid target to TWEAK for treating and preventing ischemia of the brain. Further, the PTO discredited Applicants' response because Applicants allegedly relied upon citation to legal authorities without explaining how the facts in the authorities "relate to the instant case." *Id.* Because Wiley still does not support the rejection, Applicants respectfully traverse the rejection.

In contrast to the PTO's point of view, Wiley relates to method of inhibiting angiogenesis by using TWEAK receptor antagonists including, among other things, antisense nucleic acids (para. 0075, page 6, and page 23 (claims 5-6) of Wiley). However, nothing in Wiley specifically discloses or suggests the use of antisense molecules that are directed against TWEAK, or the use of a siRNA directed against TWEAK or the TWEAK receptor.

Further undermining the rejection is disclosure in Wiley on the inhibition of angiogenesis by decreasing the level of TWEAK receptor gene expressions, *e.g.*, by the use of antisense molecules. *See* Wiley at para. 0101. Yet, the disclosure concerning treatment of diseases including ischemia of the heart, liver, or brain (*i.e.*, stroke), clearly pertains to compositions that promote angiogenesis. *Id.* at para. 0106.

Thus, contra to the PTO's characterization of Wiley, the reference does not teach a method for treating or for prophylaxis of stroke by administering to a patient an antisense nucleic acid sequence or siRNA that inhibits the expression of TWEAK in neural cells. Rather, Wiley teaches that stroke can be treated by promoting angiogenesis, a process which clearly contradicts the inhibition of TWEAK gene expression by the use of antisense oligonucleotides or siRNAs. Accordingly, Wiley does not anticipate the claimed method. Applicants respectfully request withdrawal of the rejection, therefore.

**B. The Claims Are Non-obvious In View of Wiley, Bass, and Elbashir**

The PTO also maintained its rejection of claims 17, 21, and 30 under 35 U.S.C. § 103(a) for alleged obviousness in view of Wiley, Bass, and Elbashir. *See* Office Action at page 3. The explained that it failed to discern any reasons given by Applicants as to why Bass does not rectify the deficiencies of Wiley. Further, the PTO credits the cited references with providing a reasonable expectation of success because Bass allegedly teaches that siRNAs are more robust than antisense nucleic acids for target inhibition; hence, on this premise the skilled person allegedly would have such an expectation "in using using siRNAs in place of the antisense nucleic acids taught by Wiley." *Id.* Because the cited publications do not support the PTO's reasoning or conclusion, Applicants respectfully traverse the rejection.

As discussed above, Wiley does not anticipate the claims because the reference ties treatment of stroke to the promotion of angiogenesis by antisense nucleotides or siRNAs, which relates to a mechanism quite the opposite of inhibiting TWEAK gene expression as recited in the claims. Thus, a skilled person practicing the claimed invention actually would proceed in manner contrary to what is taught by Wiley, as concerns the treatment or

prophylaxis of stroke. Such is evidence of non-obviousness. *See* MPEP 2145(X)(D)(3) (proceeding in a manner contrary to accepted wisdom is evidence of non-obviousness).

Accordingly, it is irrelevant whether Bass allegedly highlights siRNAs over antisense nucleic acids: Bass simply fails to controvert teaching in Wiley that siRNAs or antisense nucleic acids promote angiogenesis. Hence, the method of Wiley modified by Bass still would not yield the claimed method of treatment or prophylaxis of stroke. The claims are not obvious over the cited prior art, and so Applicants respectfully request reconsideration and withdrawal of the rejection.

### CONCLUSION

Having advanced credible grounds for the withdrawal of all grounds for rejection, Applicants believe that the present application is in condition for allowance. Applicants respectfully request favorable reconsideration of the application, therefore. If Examiner Pitrak believes that any outstanding issue warrants discussion, she is courteously invited to contact Applicants' undersigned attorney by telephone at the number below.

Respectfully submitted,

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The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extension of time is needed for timely acceptance of papers submitted herewith, applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extension fee to Deposit Account No. 19-0741.